REMARKS

The Office Action acknowledges the Preliminary Amendment filed on March 27, 2002 amending 8, 12-16, 20 and 24 and acknowledges that Claims 1-33 are pending.

Sequence Requirements

The present Office Action does not recognize the Preliminary Amendment and Petition for Extension of Time filed December 21, 2004 submitting an Amendment to the specification to include the sequence listing in the format required by 37 C.F.R. 1.821-1.825, and a CD containing the text of the paper copy of the sequence listing. The Response also included the required verification that no new matter has been added to the application subpart sequence requirements.

The present Office Action states that full compliance with the sequence rules is required in the Response to the present Office Action in complying with the requirements of 37 C.F.R. 1.821-1.825.

It is respectfully submitted that Applicant's previous response of December 21, 2004, as detailed immediately above, conforms with the requirements of 37 C.F.R. 1821-1.825. Applicant respectfully submits herewith as Attachment A, a printout of the file history of the present application from PAIRS, Patent Application Information Retrieval System, showing that on January 5, 2005, the Patent Office entered the submission of December 21, 2004 stating that the CRF is good technically and has been entered into the database. The designation of CRF refers to the Computer Readable Form in full compliance with the sequence rules. Further evidence of the

completion and satisfaction of this requirement in accordance with the sequence rules can be found in Attachment A which further includes a sheet entitled "raw sequence listing" and certifies that the subject listing has been "entered" on the record in this case and, therefore, is in full compliance with the stated requirements.

The Examiner is respectfully requested to acknowledge that the sequence requirements stated in the present Office Action have previously been fulfilled.

Election/Restriction

It is noted that the Examiner has made final the restriction requirement and has examined claims 1-4, 13-17, 22-25, 32 and 33 and has withdrawn claims 5-12, 18-21 and 26-31.

Applicant respectfully submits that Examiner has not substantiated reasons for the groupings I-V and applicant does not agree with the Examiner's position as taken in the present Office Action pertaining to Restriction Requirement. Nevertheless, in order to facilitate examination and issuance of claims to allowable subject matter, this present response addresses the rejection of claims 1-4, 13-17, 22-25, 32 and 33.

Information Disclosure Statement

It is noted in the Office Action that the Information Disclosure Statement filed on 3/27/02 is said to fail to comply with 37 C.F.R. 198(a)(2) which requires a legible copy of each cited foreign patent document.

An Information Disclosure Statement is being submitted herewith that includes abstracts of articles previously identified in the Information Disclosure Statement filed on 3/27/02.

Informalities noted in the Office Action

Page three of the Office Action cites an objection to the specification in line one of page 32 with regard to the spelling of the word "determinants".

A photocopy of page 32 is being provided herewith in Attachment B. It is not seen that the word "determinants" is spelled wrong in the aforesaid line one at page 32.

The Office Action states that the word "determination" is misspelled in line one of Table 6. A photocopy of Table 6 at page 39 is attached in Attachment B and it is seen that the word "determinants" is spelled properly.

The Office Action at page four says that there are letters missing in the word "comparative" in the title of Table 7. Page 42 Table 7 is attached hereto in Attachment B and it is respectfully submitted that the word "comparative" is spelled properly.

On page 40 of the Office Action, it is said that the word "stool" in Table 8 is misspelled.

Page 47 containing table 8 is attached hereto in Attachment B and it is respectfully submitted that the word "stool" is correctly spelled.

Claim Objection

There is an objection to claim 33 with regard to the word "AN" being used whereas the word "A" should be used. Appropriate correction has been made in claim 65 which replaces claim 33.

Rejection of Claims under 35 U.S.C. § 112

Claims 1-4, 13-17, 22-25 and 32-33 are rejected under 35 U.S.C. § 112 second paragraph on the basis that enhanced clarity is required. More specifically, claims 1 and 22 are said to be indefinite based on the appearance of the term "similar" and this also affects dependent claims 2-4, 13-17, 23-25 and 32-33.

Claim 1 has been replaced with claim 34 and claim 22 has been replaced with claim 54. New claims 34 and 54 do not contain the term "similar" and withdrawal of this rejection is respectfully submitted. Attachment C, Table A presents the original claims and the corresponding new claims for the Examiner's convenient reference.

Claim 17 now replaced by new claim 49 was rejected under 35 U.S.C. § 112 on the basis that it does not set forth steps involved in a method. Claim 49 as presented herewith complies with the stated requirement and withdrawal of this rejection is respectfully requested.

It is respectfully submitted that new claims 34-37, 45-49, 54-57 and 64-65 which replace corresponding claims 1-4, 13-17, 22-25 and 32-33 conform with all requirements of 35 U.S.C. § 112.

Rejection of Claim 17 under 35 U.S.C. § 101

Claim 17 was rejected on the basis that it did not recite a process and, therefore, was not a proper claim.

Claim 49 which replaces claim 17 recites a methods step and therefore is submitted to meet the requirements. Therefore, withdrawal of this rejection is respectfully requested.

Rejection of Claims under 35 U.S.C. § 112

Claims 1-4, 13-17, 22-25 and 32-33 were rejected under 35 U.S.C. § 112 first paragraph for failing to comply with written description requirement.

Applicants do not acquiesce to the correctness of this rejection on the basis set forth in the Office Action. The teachings of the present invention are read too narrowly. However, for the purpose of further enhancing clarity for issuance of claims to allowable subject matter, claim 34 presented herewith replaces claim 1 and recites as follows:

> A purified and isolated peptide, pE2, consisting of an amino acid sequence identified by SEQ ID NO: 2, homodimers or derivatives thereof having extensions, substitutions, insertions and/or deletions of the amino acid sequences defined by SEQ ID NO:2 provided that they preserve immunochemical reactivity to HEV antibodies as pE2 homodimers.

On this basis, it is respectfully submitted that the specification fully supports the invention as defined in claim 34. For this same reason, claims 35-37 (formerly 2-4), 45-49 (formerly 13-17), 54-57 (formerly 22-25) and 64-65 (formerly 32-33) which depend directly or indirectly on claim 34, are also respectfully submitted to meet all of the requirements of 35 U.S.C. § 112 and this rejection should be withdrawn.

Rejection of Claims under 35 U.S.C. § 102/103 on the Basis of Reyes 5,686,239

Claims 1-4, 13, 22, 23, 24, 25 and 33 are rejected under 35 U.S.C. 102(b) as anticipated by or, in the alternative, under 35 U.S.C. 103(a) as obvious over by Reyes et al. (US Patent No. 5,686,239A).

Claim 1 was rejected on the basis that Reyes et al. disclose a HEV peptide antigen SG3 of SEQ ID NO: 13, which comprises a carboxyl terminal 327 amino acids of HEV ORF2, and contains 100% identical amino acids of peptide pE2 of SEQ ID NO: 2 except the last three amino acid residues on the C-terminus of pE2.

New claim 34 replaces claim 1 and the term of "comprising" in the new claim 34 has been replaced with "consisting of" as indicated above which defines pE2, homodimers and derivatives thereof, and the peptide to be protected therein differs from HEV peptide antigen SG3 of SEQ ID NO: 13. Thus, it is not anticipated by US Patent No. 5,686,239A.

Further, the main claim, new claim 34, defines an anti-HEV reactive pE2 homodimer and also derivatives of pE2, which also form homodimers of the same or similar anti-HEV reactivity as pE2 homodimer. The key, unique, new and non-obvious feature of the claims is homodimers, which are immunologically reactive with anti-HEV antibodies present in serum samples, taken from patients who are having hepatitis E or are recovering from hepatitis E. The immunologic reactivity referred to is demonstrated by immunoblotting or Western blotting.

Reyes does not teach or suggest the features defined by claim 34. Thus, it is respectfully requested that the rejection on the basis of Reyes under 102/103 be withdrawn.

Note that claims 24 and 25 were incorrectly included in this grouping in the Office Action and there is no basis to reject claims 24 and 25. They are allowable as per page 11 of the Office Action. Thus, claims 24 and 25 should have been "objected to".

For the reasons given with respect to claim 34, claims 35-37 (see original 2-4), and claims 45 (13), 54-56 (22-24) and 65 (33) which depend directly or indirectly on claim 34 (1) are patentable over Reyes.

Rejection of Claims under 35 U.S.C. 102 on the Basis of Reyes 5,741,490 (B) or Reyes 5,770,689 (C).

Claims 1-4, and 13-17 are rejected under 35 U.S.C. 102(b) as being anticipated by Reyes et al. (B) (US patent No. 5,741,490A) or Reyes et al. (C) (US Patent No. 5,770,689).

Claim 1 was rejected on the basis that both Reyes et al. (B) and (C) teach an immunogenic composition comprising a HEV antigen polypeptide of HEV ORF2 or C-terminal peptide from HEV ORF2, wherein the polypeptide is SEQ ID NO: 13, 15 or 17, and each of them comprises a fragment that has 100% identity to the claimed pE2 antigen.

New Claim 34 replaces claim 1 and the term of "comprising" in the new claim 34 has been replaced with "consisting of" as indicated above, which defines pE2, homodimers and derivatives thereof and the peptide to be protected therein differs from HEV antigen of SEQ ID NO: 13, 15 or 17. Thus, it is not anticipated by said US patents.

Further, the main claim, new claim 34, defines an anti-HEV reactive pE2 homodimer and also derivatives of pE2, which also form homodimers of the same or

similar anti-HEV reactivity as pE2 homodimer. The key, unique, new and non-obvious feature of the claims is homodimers, which are immunologically reactive with anti-HEV antibodies present in serum samples, taken from patients who are having hepatitis E or are recovering from hepatitis E. The immunologic reactivity referred to is demonstrated by immunoblotting or Western blotting.

Reyes (B) or (C) do not teach or suggest the features defined by claim 34. Thus, it is respectfully requested that the rejection on the basis of Reyes under 102 be withdrawn.

For the reasons given with respect to claim 34, claims 35-37 (2-4) and claims 45-49 (13-17) which depend directly or indirectly on claim 34(1) are patentable over Reyes (B) and (C).

Rejection of Claims under 35 U.S.C. § 102 on the Basis of Khudyakov

Claims 1, 4, 32 are rejected under 35 U.S.C. 102(b) as being anticipated by Khudyakov et al. (Virol. 1994, pp. 390-393).

Claim 1 was rejected on the basis that Khudyakov et al. disclose several peptide antigens that are all fragments with 100% identical to the amino acid sequence fragment of SEQ ID NO: 2 (See Table 1). All of these peptides except two (No. 30 and No. 38) are antigen determinants.

New claim 34 replaces claim 1 and the term of "comprising" in the new claim 34 has been replaced with "consisting of" as indicated above, which defines pE2, homodimers and derivatives thereof, and one peptide to be protected therein differs

from HEV peptide antigen of SEQ ID NO: 2. Thus, it is not anticipated by said document.

Further, the main claim, new claim 34, defines an anti-HEV reactive pE2 homodimer and also derivatives of pE2, which also form homodimers of the same or similar anti-HEV reactivity as pE2 homodimer. The key, unique, new and non-obvious feature of the claims is homodimers, which are immunologically reactive with anti-HEV antibodies present in serum samples, taken from patients who are having hepatitis E or are recovering from hepatitis E. The immunologic reactivity referred to is demonstrated by immunoblotting or Western blotting.

Khudyakov et al. does not teach or suggest the features of new claim 34. Thus, it is respectfully requested that the rejection on the basis of Khudyakov under 102 be withdrawn.

For the reasons given above with respect to claim 34, claims 37 (4), 64 (32) are patentable over Khudyakov.

Rejection of Claims Under 35 U.S.C. § 102 on the basis of Li et al. U.S. Patent No. 6,514,690B1

Claims 1-4, 13-17, 22 and 33 are rejected under 35 U.S.C. 102(e) as being anticipated by Li et al. (US Patent No. 6,514,690B1).

Claim 1 was rejected on the basis that Li et al. disclose a peptide antigen of SEQ ID NO: 18 that comprises a fragment with 100% homology to the claimed peptide E2, wherein the peptide antigen is produced as a glutathione-transferase fusion protein.

New claim 34 replaces claim 1 and the term "comprising" in the new claim 34 has been replaced with "consisting of" as indicated above, which defines pE2, homodimers and derivatives thereof and the peptide to be protected therein differs from HEV peptide antigen of SEQ ID NO: 18. Thus, it is not anticipated by Li et al.

Further, the main claim, new claim 34, defines an anti-HEV reactive pE2 homodimer and also derivatives of pE2, which also form homodimers of the same or similar anti-HEV reactivity as pE2 homodimer. The key, unique, new and non-obvious feature of the claims is homodimers, which are immunologically reactive with anti-HEV antibodies present in serum samples, taken from patients who are having hepatitis E or are recovering from hepatitis E. The immunologic reactivity referred to is demonstrated by immunoblotting or Western blotting.

Li et al. does not teach or support the features of claim 34(1). Thus, it is respectfully requested that the rejection on the basis of Li et al. under 102 be withdrawn.

For the reasons given with respect to claim 34, claims 35-37 (2-4), 45-49 (13-17), 54(22) and 65(33) are patentable over Li et al.

Allowable Claims 24-25

Claims 24 and 25 are said to be allowable except for dependence on claim 22. Claim 66 presented here is an independent claim which contains the features of respective claims 24 and 25 in the alternative and also contains the features of claim 22. Any claim rejections under 35 U.S.C. § 112 have been addressed in new claim 66 so as to further enhance clarity.

CONCLUSION

It is believed that all of the stated grounds of rejection have been properly traversed, accommodated, or rendered moot. Applicant therefore respectfully requests that the Examiner reconsider and withdraw all presently outstanding rejections. It is believed that a full and complete response has been made to the outstanding Office Action, and as such, the present application is in condition for allowance. Thus, prompt and favorable consideration of this amendment is respectfully requested. If the Examiner believes that personal communication will expedite prosecution of this application, the Examiner is invited to telephone the undersigned at (248) 641-1600.

Respectfully submitted,

Dated: 7 September 05

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